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Docket No: 5407/1J328US1

07278

PATENT TRADEMARK OFFICE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Daryl REAL; Mike D. TOKACH; Steve S. DRITZ; Jim L. NELSEN;
Robert D. GOODBAND; Jason WOODWORTH; Kevin Q. OWEN

Serial No.: 10/087,198

Art Unit: 1614

Confirmation No.: 8576

Filed: March 1, 2002

Examiner: Donna A. Jagoe

For: METHOD OF ENHANCING REPRODUCTIVE PERFORMANCE IN SOWS

RESPONSE TO OFFICE ACTION

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

Sir:

The Office action of December 18, 2002 and the references cited therein have been received and carefully studied. Reconsideration is respectfully requested.

As will be recalled, the subject application is directed to a method of improving the reproductive performance of sows which comprises feeding to the sows during gestation

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and, optimally, during lactation, breeding and/or prebreeding L-carnitine or a salt thereof in combination with a trivalent chromium salt. It is acknowledged at the outset that both L-carnitine and certain salts of trivalent chromium, e.g., chromium picolinate, have been used individually to improve the reproductive performance of sows. This is amply shown in the references cited in the Information Disclosure Statements filed herewith as will be further discussed below. On the other hand, applicants have discovered that a combination of these two materials results in improved aspects of reproductive performance that were never realized or contemplated by the feeding of each of the components individually. The data set forth in the patent application show that synergistic response in key reproductive areas was obtained.

Turning now to the Office action, claims 1 through 15 have been rejected under 35 U.S.C. 102(a) as being anticipated by Nelssen et al., the Swine Update article of Spring 2001. Applicants acknowledge that this work is relevant to the subject invention, but wish to point out that the publication represents work done by the inventors of the subject application. Furthermore, it will be noted that the subject application is based on a foreign application filed on April 24, 2001 and a provisional application filed on May 17, 2001. Both of these dates are prior to the publication of the Nelssen et al. publication. In addition, the actual filing date of the subject application, namely, March 1, 2002, is less than one year prior to the publication of Nelssen et al. Specifically, Nelssen et al. was published on or about June 5, 2001 and certainly not before May 22, 2001, the date on which Nelssen et al. was sent by Kansas State University for reproduction.

Attached hereto is a Declaration of Jason Woodworth, Technical Service Manager of the Lonza Group, one of the assignees of the subject application. In this paper Dr. Woodworth testifies that Nelssen et al. was sent for duplication on May 22, 2001 with a due date for copies to be made on June 5, 2001. Attached to Dr. Woodworth's Declaration is a copy of a Production Services/Duplicating Work Order of Kansas State University requesting that the Swine Update-Spring 2001 manuscript be duplicated for subsequent publication. This Production Services/Duplicating Work Order No. 822-01 is a work order of the Kansas State University Publications Unit. It will be noted that some 2100 copies were requested.

The Declaration of Jason Woodworth, a co-inventor, attests that the invention described in Nelssen et al. is the same invention as that described in the subject application and that the invention was made by the inventors named herein. In light of the foregoing, it is respectfully submitted that the declaration overcomes the rejection set forth under 35 U.S.C. 102(a) and, pursuant to MPEP 716.10, the rejection should be withdrawn.

In paragraph 1 on page 3 of the Office action, all of the claims are rejected under 35 U.S.C. 103(a) over the J. Arthington article. As the Examiner notes, the Arthington reference teaches the combination of L-carnitine and chromium picolinate to increase lean gain potential by increasing the amount of energy a pig receives during this energy-dependent phase of growth. But this is wholly unrelated and even antithetical to the objectives of the subject application where gestating and lactating sows are of concern.

Arthington's data is based on young growing pigs where high growth rates for muscle deposition are desirable. Gestating and lactating sows, however, have totally different nutritional requirements. This is clearly established by the different nutritional requirements described in the National Research Council's National Requirements of Swine 1998 (#22 from the IDS of Paper No. 3). (Note particularly the amino acid and vitamin and mineral requirements noted in Tables 10-1, 10-2, 10-5 and 10-6 for growing pigs; and these requirements for gestating sows in Tables 10-7, 10-8, 10-11 and 10-12; and for lactating sows in Tables 10-9, 10-10, 10-11 and 10-12.) Sows in gestation must provide nutrients to the developing fetus and lactating sows must produce milk. Weight gain is detrimental to sows, a function quite the opposite of what is required of growing finishing pigs. Accordingly, one skilled in the art would not consider relevant the nutritional practices applied to growing pigs for sows, especially in this case, since the nutritional intake for sows must be restricted.

The inventors herein have discovered that, in the case of sows, the combined effects of L-carnitine and chromium are unexpectedly different than in the case of growing pigs. They discovered that this combination affects the reproductive system by changing various metabolisms that in turn affect reproductive hormone concentrations. Obviously, there is nothing in the teaching of the Arthington publication (it being restricted to growing pigs) that would suggest any effect on reproductive performance, let alone the specific effects applicants have discovered.

In paragraph 2, beginning on the bottom of page 4 of the Office action, the Examiner rejects all of the claims under 35 U.S.C. 103(a) as unpatentable over Blum et al. (# 8 from the IDS of Paper No. 3) and Lindemann et al. (#17 from the IDS of Paper No. 3).

It should be noted that, in the case of these two references, the Blum U.S. patent issued on June 5, 2001 and Lindemann et al.'s disclosure was presented on August 29, 2001. It is respectfully submitted that these references are not proper since, as noted above, the European application on which this application bases priority was filed on April 24, 2001 and the provisional application on May 17, 2001, both of which antedate the effective date of these two references. Furthermore, the Blum U.S. patent cannot be cited under 35 U.S.C. 102(e) since this patent was not "an application for a patent . . . by another filed in the United States." Both the subject application and the Blum reference are co-owned by Lonza Inc. and the Kansas State Research Foundation.

Notwithstanding the foregoing, it is respectfully submitted that an analogous rejection may be made by the Examiner based, for example, on the 1994 and 1995 Lindemann publications and/or the Purser publication (respectively, #1, #3 and #6 in the IDS filed on June 12, 2002) and the Hagen publication (#4 in the IDS filed on November 25, 2002). With respect to Blum, the corresponding PCT Publication PCT/US97/22215 containing essentially the identical text was published on June 11, 1998 and therefore would be an appropriate citation. This reference and two related publications by the inventors are submitted herewith. These references were not submitted earlier because the subject matter is the same as Blum,

but it was not realized at the time of submitting the earlier IDS that Blum's U.S. patent was published after the effective date of this application.

Notwithstanding, it is respectfully submitted that, despite the prior art showing the use of trivalent chromium and carnitine used separately to enhance reproductive performance of sows, one skilled in the art would not have expected that the combination of these two components would result in still further and unexpected improvements.

By way of introduction, it will be understood that one of the most important economic factors affecting profitability of a swine farm is number of pigs born per sow. This is particularly important because, over time, input costs such as facilities, feed and labor have increased while profit margins have decreased. Therefore, to remain competitive, swine producers must be as efficient as possible. For this reason, the subject invention is of utmost importance today.

As a general matter, a sow will be mated when she is about 9 to 10 months of age and, over her productive lifetime, will typically have 4 to 6 litters and ideally wean over 9 pigs per litter. Unfortunately, too many sows do not reach this goal. There are numerous reasons for this, but the primary factors include a low conception rate (failure to conceive after mating, often termed "farrowing rate") and a long period between weaning and becoming pregnant again. Not only is it important to become pregnant, but it is important to become pregnant quickly (first service farrowing rate). This will allow the sow to have more litters per year (an indicator of efficiency) and raise the number of pigs born.

To gather the data for the subject application, the inventors went into a commercial swine farm and assigned sows, immediately **after** mating, to one of four treatments. The sows were of various ages and parities. They were followed from mating through pregnancy and lactation (what is described in the text as parity 1) and through the subsequent mating, pregnancy and lactation (parity 2). The unique and totally unexpected finding was that, when sows were mated the second time, the sows fed carnitine or chromium conceived somewhat more frequently, but also sows fed the combination of the two conceived much more frequently. This response was most notable in the second mating (or parity) because treatments were only administered **after** sows were mated at the start of the study. Arguably, if the sows had the benefit of being fed the carnitine and chromium diets before they were mated at the start of the study, the response in parity 1 would have been similar to that in parity 2.

The data set forth in Table V unequivocally reveal that, by feeding both carnitine and chromium, the number of sows that become pregnant increases. Therefore, with a greater percentage of the sows becoming pregnant, there is net increase in the number of total litters, and thus the number of pigs a sow will produce in her lifetime. More specifically, in the second parity (the second litter the sows produced during the experiments) 91% of the sows became pregnant vs only about 80% where only one of the components was added. See Table V, page 15, line 30. In other words, for every 100 sows, those fed the combination of carnitine and chromium would be expected to have 10 extra litters. This has huge economic ramifications to swine farmers.

Additionally, starting with the number of sows at the beginning of the study, taking into account the different percentages of those that conceived during the study, and multiplying by the number of pigs that were born after they became pregnant, the total pigs produced per sow over the two parities was determined. Control sows had an average of 13.9 pigs during the entire study, sows fed carnitine had an average of 16.3 pigs during this period, sows fed chromium had an average of 16.2 pigs, and, lastly, sows fed both carnitine and chromium had 17 pigs born alive. This is illustrated in Table V, page 16, line 22.

To illustrate the significant economic importance of this effect alone, the following calculation is presented. It assumes the value of a weaned pig at \$20, a very conservative figure. The return or profit to the farmer for each sow compared to no supplementation is shown below.

<u>Item</u>	<u>Control</u>	<u>Carnitine</u>	<u>Chromium</u>	<u>Both</u>
Value of Live Pigs	\$ 278	\$ 326	\$ 323	\$ 341
Added Income	--	\$ 48	\$ 45	\$ 63

Using, for example, a sow producer having 64,000 sows (the average number of sows in the largest forty producers) using the feed supplement of the invention, annual savings of over \$4 million would be realized.

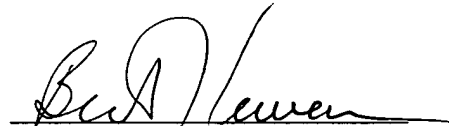
It is because of these economic savings that Lonza, an assignee of the instant application, has commercialized a feed supplement known and sold under its trademark, CARNICHROME. Since it was first offered for sale in the spring of 2001, it has become a commercial success and has become an important factor in sow nutrition.

To conclude, because the combination of carnitine and chromium substantially improves conception (farrowing rate) in sows, suggesting that the two components are working via two different mechanisms of action, there is a large and substantial economic benefit to their use in commercial swine production. These findings are wholly unexpected from a reading of the prior art and therefore the products and processes claimed are clearly entitled to patent protection.

In light of the foregoing, it is respectfully submitted that the subject application is now in condition for allowance. A Notice to that effect will be greatly appreciated.

Respectfully submitted,

Date: April 1, 2003



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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 5407/2J328-W	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. PCT/US 02/ 12921	International filing date (day/month/year) 23/04/2002	(Earliest) Priority Date (day/month/year) 24/04/2001
Applicant LONZA LTD.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/12921

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A23K1/16 A23K1/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 A23K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, CAB Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	C.D. HAGEN ET AL.: "Effect of dietary chromium tripicolinate on productivity of sows under commercial conditions" SWINE HEALTH AND PRODUCTION, vol. 8, no. 2, 2000, pages 59-63, XP001113109 DES MOINES, IA, US ISSN: 1066-4963 cited in the application the whole document	1-12
Y	WO 98 24328 A (GOODBAND ROBERT D ; UNIV KANSAS STATE (US); NELSEN JIM L (US); MUS) 11 June 1998 (1998-06-11) the whole document	1-12

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

27- September 2002

Date of mailing of the international search report

07/10/2002

Name and mailing address of the ISA

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Authorized officer

Dekeirel, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/12921

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01 17525-A (HASSEN KEN) 15 March 2001 (2001-03-15) page 7, line 8 - line 11 example 1 claims 7-11 ---	13-15
Y	DE 199 07 586 A (BONERMO HEALTH GMBH) 24 August 2000 (2000-08-24) claim ---	13-15
A	<i>already cited</i> A.T. WAYLAN ET AL.: "The effects of swine dietary supplementation of modified tall oil, chromium nicotinate, and L-carnitine on longissimus muscle quality characteristics and display color stability" JOURNAL OF ANIMAL SCIENCE, vol. 77, no. Suppl. 1, 1999, page 50 XP008008163 NEW YORK, NY, US ISSN: 0021-8812 cited in the application page 50, Abstract 104 -----	1-12

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 02/12921

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9824328	A	11-06-1998	AU	726346 B2	02-11-2000
			AU	5464698 A	29-06-1998
			EP	0951218 A1	27-10-1999
			WO	9824328 A1	11-06-1998
			US	6451856 B1	17-09-2002
			US	6242487 B1	05-06-2001
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WO 0117525	A	15-03-2001	AU	7347000 A	10-04-2001
			EP	1218001 A1	03-07-2002
			WO	0117525 A1	15-03-2001
			US	2002111383 A1	15-08-2002
<hr/>					
DE 19907586	A	24-08-2000	DE	19907586 A1	24-08-2000
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